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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,223	12/06/1999	DAVID WALLACH	WALLACH 24	9660

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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 05/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,223	WALLACH ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-8,11,12,14-17,19,22-24,29-37 and 40-51* is/are pending in the application.

4a) Of the above claim(s) *12,14-17,19,22,29-37,40-43,49 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8,11,23,24,44-48 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant adds new claim 51, which is related to claims 5-8, 11, 23, 24, 44-48 and is not new matter.

Accordingly, claims 5-8, 11, 23, 24, 44-48 and 51 are being examined.

RESTRICTION

Applicant argues that claims 40-43 drawn to the B1 protein encoded by the claimed polynucleotide at least should be examined with the elected DNA claims. Applicant argues that the protein should be rejoined with the encoding DNA, according to PCT Administrative Instructions, Annex B, Unity of Invention, Part 2, because the protein and the DNA sequence exhibit corresponding special technical features.

This is not found to be persuasive, because the structure of the claimed polynucleotides and the encoded B1 protein is different, and thus could not constitute shared special technical features.

The requirement is still deemed proper and was made FINAL, for reasons set forth in previous Office action.

Accordingly, claims 5-8, 11, 23, 24, 44-48 and 51 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Rejection under 35 USC 112, second paragraph of claims 23, 24, 45-47, pertaining to being depending on non-elected claims remains for reasons already of record in paper No.9. New claim 51 is rejected for the same reasons already of record in paper No.9.

Applicant argues that since the restriction issue has not been resolved, the 112, second paragraph rejection of claims 23, 24, 45-47 for depending on non-elected claims is inapplicable. Furthermore, the fact that the claims are dependent on non-elected claims does not make them indefinite.

Applicant's arguments set forth in paper No.11 have been considered but are not deemed to be persuasive for the following reasons:

Rejection remains, because the restriction requirement is still deemed proper and is therefore made FINAL. Further, claims 23, 24, 45-47, 51 are indefinite, because MPEP 821 teaches that "because applicant believes the claims are readable on the elected invention and the examiner disagrees, the metes and bounds of the claim(s) cannot be readily ascertained, rendering the claim(s) vague and indefinite within the meaning of 35 USC 112, second paragraph".

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

1. Claims 23, 24, 46-47 are indefinite, because claim 40 to which claims 23, 24, 46, 47 depend recites the language "an amino acid sequence", which encompasses a sequence comprising two amino acids.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

Claims 5-8, 11, 44, 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 5-8, 11, 44, 46 are drawn to a DNA sequence encoding an anolog of SEQ ID NO:1 "having no more than ten changes" in the amino acid sequence of SEQ ID NO:1, a vector and a host cell comprising said DNA sequence, and a method of producing a polypeptide which potentiates cell death using said host cell.

The specification does not disclose a DNA sequence encoding an analog of SEQ ID NO:1, having the limitation of "having no more than ten changes" in the amino acid sequence of SEQ ID NO:1.

REJECITON UNDER 35 USC 101, NEW REJECTION

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement

thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5-8, 11, 23-24, 44-48, 51 are rejected uner 35 USC 101 because the claims are directed to non-statutory subject matter.

The DNA sequence and the encoded polypeptide as claimed have the same characteristics and utility as a DNA sequence and a polypeptide found naturally and therefore do not constitute patentable subject matter. In the absence of the hand of man, the naturally occurring DNA sequence and polypeptide is considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Amendment of the claims to recite "an isolated DNA sequence" or " an isolated polypetide" is suggested to overcome this rejection.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Rejection under 35 USC 112, first paragraph of claims 5-8,11, 44 (c), 47, 48, pertaining to lack of a clear written description of a DNA sequence encoding a fragment of SEQ ID NO:1, which fragment potentiates cell death, remains for reasons already of record in paper No.9.

Applicant argues that it is not a burden to make and screen for said fragments by removing codons from either end of the full length polynucleotide and see if they express a polypeptide which potentiate cell death.

Applicant's arguments set forth in paper No.11 have been considered but are not deemed to be persuasive for the following reasons:

This is a written description rejection and not an enablement rejection. Although one could screen for said fragments, the structure of said fragments, or their functional characteristics coupled with a known correlation between function and structure, or the conserved regions which are critical for the structure and function of the claimed fragments, are not disclosed in the specification.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. Rejection under 35 USC 112, first paragraph of claims 5-8,11, 44-47, pertaining to lack of enablement of a DNA sequence "encoding" SEQ ID NO:1, an analog, or fragment thereof, remains for reasons already of record in paper No.9. Claims 23-24, 48 and new claim 51 is rejected for the same reasons already of record in paper No.9.

Applicant argues that it does not matter whether the protein was isolated from nature or made recombinantly. This issue is irrelevant to the enablement of the claims. Further, Applicant argues that all evidence suggests that the claimed polypeptide is found *in vivo*, and the few exceptions to the rules cited by the Examiner does not change the general rule that one would expect expression of B1 at least in some cells at some time.

Applicant's arguments set forth in paper No.11 have been considered but are not deemed to be persuasive for the following reasons:

The claims are only enabled for a polynucleotide encoding the synthetic or recombinant amino acid sequence of SEQ ID NO:1. The claims however encompass a polynucleotide encoding *in vivo* the amino acid sequence of SEQ ID NO:1 or its

analogs, i.e. the presence of SEQ ID NO:1 or its analogs in various tissues. This enablement issue is important when one considers the use of SEQ ID NO:1 or its analogs for detection of diseases such as those associated with abnormal expression of SEQ ID NO:1 or its analogs. As discussed in the previous Office action, translational control is common for most proteins, and the expression of mRNA does not dictate nor predict the translation of such mRNA into a polypeptide as taught by Alberts et al, Shantz et al, McClean et al, and Fu et al, all of record. Further, Applicant has not recited any evidence supporting Applicant opinion that all evidence suggests that the claimed polypeptide is found *in vivo* and the general rule that one would expect expression of B1 at least in some cells at some time.

2. Rejection under 35 USC 112, first paragraph of claim 11, pertaining to lack of enablement of a method for producing "any polypeptide" that potentiates cell death, remains for reasons already of record in paper No.9.

Applicant argues that the claims only reads on a method for producing those polypeptides that potentiate cell death which one can obtained by expressing a host cell of claim 8. The word "any" does not appear in the claim.

Applicant's arguments set forth in paper No.11 have been considered but are not deemed to be persuasive for the following reasons:

Although the word "any" is not in the claim 11, the language "a polypeptide that potentiates cell death" encompasses any polypeptide that potentiates cell death, which is not necessary the claimed amino acid sequence of SEQ ID NO:1. Moreover, the claim does not specify that wherein said polypeptide that potentiates cell death is

obtained by expressing a host cell of claim 8. The claim as written thus encompasses a method for producing "any polypeptide" that potentiates cell death, including those polypeptides that are not necessary the claimed amino acid sequence of SEQ ID NO:1, such as caspases, the structure of which is completely different from SEQ ID NO:1.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

If Applicant could overcome the above 112, first paragraph rejections, claims 23, 24, 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vector encoding SEQ ID NO:1, and an antisense sequence of an mRNA sequence encoding SEQ ID NO:1, does not reasonably provide enablement for a vector encoding a "derivative" of SEQ ID NO:1, and an antisense sequence of an mRNA sequence encoding a derivative SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 23, 24, and 51 are drawn to 1) a vector encoding a polypeptide of claim 40, which includes a derivative of SEQ ID NO:1, and 2) an antisense sequence of an mRNA sequence encoding a polypeptide of claim 40, which includes a derivative of SEQ ID NO:1.

Claims 23, 24, and 51 encompass a vector encoding a derivative of SEQ ID NO:1, and an antisense sequence of an mRNA sequence encoding a derivative SEQ ID NO:1.

The present specification (p.31, lines 12-27), and Applicant response on page 13, 20 discloses that derivatives include only those derivatives that do not change one amino acid to another, and thus derivatives only refer to modification of the amino acids, and could not be encoded by a DNA sequence.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention.

REJECTION UNDER 35 USC 102, NEW REJECTION

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 51 is rejected under 35 U.S.C. 102(b) as being anticipated by Siyanova, et al, Genbank Sequence Database (Accession I49118), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available on 1994.

Claim 51 is drawn to an antisense sequence of at least a part of an mRNa sequence encoding a polypeptide of SEQ ID NO:1.

Siyanova, et al teach a peptide of 66 amino acids in length, which is 100% similar to the claimed SEQ ID NO:1, from amino acid 160 to 168, under MPSRCH

sequence similarity search (MPSRCH search report, 2002, us-09-445-223-1.rpr, page 2).

Given the polypeptide sequence taught by Siyanova, et al, one of ordinary skill in the art would immediately envision the claimed antisense oligonucleotide sequence.

REJECTION UNDER 35 USC 103, NEW REJECTION

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Siyanova, et al, 1994, *supra*, in view of Johnstone and Thorpe (Immunochemistry in Practice, 2nd Ed., 1987, Blackwell Scientific Publications, Oxford, pages 49-50).

The teaching of Siyanova, et al has been set forth above.

Siyanova, et al however do not teach a pharmaceutically acceptable excipient.

Johnstone and Thorpe teach that it was common practice in the art at the time of applicant's invention to formulate compositions of antibodies and PBS, which is considered to be an acceptable carrier for storage of antibodies, p. 49 and 50.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include a pharmaceutically acceptable excipient in the composition because Johnstone and Thorpe teach that it was common practice in the art at the time of applicant's invention to formulate compositions of antibodies and PBS,

which is considered to be an acceptable carrier for storage of said compositions, p. 49 and 50. One of ordinary skill would have been motivated to do so in order to develop compositions suitable for storage. Finally, it has been held by the Court that a compound and a carrier are obvious, if it is obvious in the art to utilize a carrier with related compounds. See *In re Rosicky*, 125 USPQ 341 (CCPA 1960).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

May 18, 2002